A case of idiopathic diabetes insipidus presented with bilateral hydroureteronephrosis and neurogenic bladder: A pediatric case report and literature review

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Abstract

Diabetes insipidus (DI) is a condition with heterogeneous clinical symptoms characterized by polyuria (urine output >4 mL/kg/hr) and polydipsia (water intake >2 L/m²/d). In children, acquired nephrogenic DI (NDI) is more common than central DI (CDI). Diagnosis is based on the presence of high plasma osmolality and low urinary osmolality with significant water diuresis. A water deprivation test with vasopressin challenge, though has limitations, is done to differentiate NDI from CDI and diagnose their incomplete forms. Neonates and young infants are better managed with hydration therapy alone. Older children with CDI are treated with desmopressin (1-deamino-8-D-arginine vasopressin, dDAVP). Its oral form is safe, highly effective and has dosing flexibility. We report a case of an 8-year-old male patient with CDI with severe bilateral non-obstructive hydronephrosis and megaureter. Dramatic clinical and radiological responses to dDAVP treatment were achieved and therapy reduced urine volume and led to marked radiological improvement in hydronephrosis.

Introduction

Essential features of diabetes insipidus (DI) include: polyuria, defined as urine output of more than 4 mL/kg/hr in children (more than 6 mL/kg/hr in neonates); polydipsia, characterized by water intake of more than 2 L/m²/d (or more than 5 L/d); and failure to thrive or growth retardation. The essential pathophysiology in central DI (CDI) involves a decrease in antidiuretic hormone (ADH) secretion as a consequence of neoplasms, autoimmune pathologies, trauma, pituitary surgery, hypoxia or ischemic encephalopathy. In nephrogenic DI (NDI), despite normal ADH secretion, kidneys are refractory to the effects of ADH. In both polydipsia and DI, water diuresis is present. However, in water and solute diuresis, excretion of solutes increases and ADH dysfunction involving either its secretion or renal response to ADH develops. With its natriuretic and ADH-antagonizing effects, atrial natriuretic peptide (ANP) should be considered in the etiology of polyuria.

Osler first described prolonged polyuria as a cause of bilateral, non-obstructive hydronephrosis in 1892. Since then, excessive urine flows and extensive dilatation of the urinary tract have been most frequently documented in young children with NDI, mostly a hereditary and X-linked disease, and also in patients with CDI and psychogenic polydipsia. Apparently, persistent large urine volumes can lead to urinary bladder distension and hypertrophy with subsequent intramural obstruction of the distal ureteral segments. With time, bladder contractility is compromised, ureteric peristalsis diminishes and large residual urine volumes worsens this functional obstructive uropathy. Excessive polyuric syndrome rarely gives rise to non-obstructive hydronephrosis, megaureter and neurogenic bladder.

Case report

We present an 8-year-old male patient with neurogenic bladder who was receiving anticholinergic treatment and using clean intermittent self-catheterization for 4 years. His personal and family history was uneventful. His parents did not describe any urinary symptom during his first 3 years, and he suffered with polyuria and polydipsia since then. During this time, the patient complained of nocturnal enuresis and therefore was admitted to our clinic. On physical examination, his body weight (25 kg), height (122 cm), arterial blood pressure (102/68 mm Hg), and pulse rate (95/min) were measured. His mental development was normal.

When his previous examination results were reviewed, we noted progressive hydroureteronephrosis (Fig. 1). His daily fluid intake and urine output were nearly 6000 cc and 5000 cc, respectively. Renal function test results, serum and
urine electrolyte values were within normal limits. Urine density was 1002. Urine and plasma osmolality measured during the early morning hours were 150 mOsm/kg/water and 310 mOsm/kg/water, respectively. The patient could not tolerate thirst. Urinary system imaging modalities revealed bilateral hydronephrosis (on ultrasonograms AP diameters of the right and left renal pelvises were measured as 21 mm and 25 mm, respectively), while voiding cystourethrogram demonstrated bilateral non-refluxive and non-obstructive megaureter, increased bladder capacity (350 cc), and postmictional residual urine (250 cc). DMSA and DTPA scanning of the ureterovesical junction revealed a right and left kidney contributing 57% and 43% to total renal functions, respectively. Following diuretic injection, we detected bilateral hydronephrosis with normal urine output. Urine specimens were collected for 24 hours and creatinine clearance was 39%. On cystourethroscopic examination, urethra was intact, bladder was trabeculated and ureteral orifices were normal in location and configuration.

Pituitary magnetic resonance imaging (MRI) (Fig. 2) examination and analyses of cortisol, TSH and fT4 were performed to detect other potentially associated pituitary disorders, and yielded normal results. Plasma ADH level was 0.5 pg/mL (normal ≥1.1 pg/mL). Thus, a diagnostic hypothesis of CDI was raised. A challenge test with a nasal dDVAP 10 μg twice a day was performed to confirm the diagnosis of CDI. A dramatic response was obtained as early as day 2 of treatment. His daily oral fluid intake was 800 cc and urine output was 1200 cc. Any treatment side effect was not detected.

Renal function tests, serum and urine electrolytes were controlled and evaluated as normal at 1, 3, 6, and 12 months of the treatment, respectively. At 1 month of treatment, single daily doses of nasal dDVAP were administered. Despite this change in treatment, treatment response was obtained. During follow-up, stepwise regression in hydronephrosis (Fig. 3) and postmictional residual urine was observed. At 12 months post-treatment, AP diameters of the right and left renal pelvises were 7 mm and 8 mm, respectively. During urodynamic examination, the patient’s bladder capacity was 270 cc with no postmictional residual urine. Urodynamic study revealed normal detrusor activity, normal bladder sensation and compliance. Renal scanning

**Fig. 1.** Magnetic resonance urography imaging of urinary tract before 1-deamino-8-D-arginine vasopressin (DDAVP) treatment (left); bilateral hydronephrosis (right).

**Fig. 2.** Pituitary magnetic resonance image.
Diabetes insipidus in a pediatric patient

results were not unremarkable. Presently, the patient has not required clean intermittent catheterization and treatment is maintained with single daily doses of nasal dDVAP.

Discussion

The signs and symptoms of DI vary with the etiology, loss of excessive amounts of free water, extreme feeling of thirst, dehydration and hypernatremia. Manifestations vary between age groups, depending on the patients’ ability to replenish water. Younger children often manifest with primary enuresis. Older children characteristically have high urine output and nocturia leading to disturbed sleep. Familial autosomal dominant forms of CDI usually start by age 5 or 6 years, but may manifest as late as the third decade. Familial autosomal recessive forms manifest in infancy and the age of presentation of Wolfram syndrome, DI, diabetes mellitus, optic atrophy and deafness syndrome (DIDMOAD) may vary.

If first urine specimen obtained in the morning has a density of 1010, then DI should be suspected. Since the urine-concentrating ability of infants is not developed fully, it is difficult to make a diagnosis based on urine density. Various studies suggest that the combination of the water deprivation test and direct ADH determination would refine the diagnosis in more than 95% of DI cases. A long dehydration period may provide not only an osmotic, but a volumetric stimuli. It has been shown that dehydration alone may induce considerable ADH-independent urine concentration. Pituitary MRI is an important tool in determining CDI etiology and should always be performed after gadolinium injection to check for abnormal enhancement within the pituitary stalk.

The therapeutic goals are primarily to reduce polyuria and decrease the feeling of thirst, so that the child is able to grow adequately and maintain a normal lifestyle. Although many patients have undergone surgical procedures to alleviate this functional obstruction, treatment should be essentially medical. Specific therapy depends on the etiology. Fluids alone can work in very young infants and neonates. As they have a high obligatory oral fluid intake, vasopressin therapy may cause hyponatremia. dDAVP is the current drug of choice for long-term therapy of CDI. This synthetic analogue has more specific antiuretic action, negligible pressor activity and a longer half-life than the native molecule. It can be given parenteral, oral or intranasal way. Although 20 times less potent than the intranasal form, oral tablets are highly effective and safe in children with more dosing flexibility. The recommended doses of dDAVP are 100 to 1200 µg/day in 3 divided oral doses. Dilutional hyponatremia, headache, hypertension and nasal congestion are some of the side effects occasionally seen.

Conclusion

In our case, dDAVP therapy reduced urine volume and led to marked radiological improvement in hydronephrosis.

Competing interests: The authors declare no competing financial or personal interests.

This paper has been peer-reviewed.

References


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